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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/389,565	09/03/1999	DAVID M. NEVILLE, JR.	14028.0290	5574

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 11/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/389,565	NEVILLE, JR. ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-33,37-39 and 43-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *31-33,37,39 and 44-47* is/are allowed.

6)☒ Claim(s) *38,43 and 48-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 9/11/06 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendments, remarks, filed 9/11/06 (which appear to be duplicates of the amendments and remarks filed 6/12/06), have been entered.

2. Claims 31-33, 37-39, 43-48-51, are pending and being acted upon.

3. In view of the overlapping and confusing nature of the previous rejections, all have been withdrawn. New rejections are set forth below. As appropriate, Applicant's arguments have been addressed.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 38, 43, and 48-51 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) In Claims 38, 43 and 50 a method for inhibiting the rejection of mismatched kidney transplant in a subject, are not supported by the specification.

B) The immunotoxin of Claim 48 comprising a truncated diphtheria toxin moiety … wherein the truncated toxin moiety

bypasses the inhibitory effect of pre-existing anti-diphtheria toxin antibodies, is not disclosed in the specification.

Regarding A), Applicant argues that support for the limitation can be found at page 40, lines 5-7.

Page 40, lines 5-7, found within Example 9, disclose, "FN18-CRM9 has also been used as an adjunct in inducing tolerance to mismatched kidney transplants". FN18-CRM9 is not the antibody of the instant claims.

Applicant cites Example 7, arguing that "It should be scientifically clear that the disclosed mechanism (T cell depletion) that inhibits rejection in the case of mismatched kidney transplants and skin allografts would produce this result in any other transplantation contexts".

As set forth previously, it is the Examiner's position that it is well-established that the requirement of the first paragraph of 35 U.S.C. 112 is not satisfied by subject matter that is not disclosed, but which might be obvious. One shows possession of an invention by describing the invention, including all claimed limitations. *Lockwood v. American Airlines*, 1966, 41 USPQ2d 1961 (CAFC 1997), makes clear "all the limitations must appear in the specification". Thus, Applicant cannot choose limitations disclosed only in a limited context, in this instance disclosed as applying to the use of the FN18-CRM9 antibody, and apply said limitations to the use of the antibody of the instant claims.

Applicant argues that "FN18-CRM9 is the rhesus monkey analog of UCHT1-CRM9". In this context Applicant appears to be arguing that FN18 is used in mismatched kidney transplant; UCHT1-CRM9 is the human version of FN18-CRM9; UCHT1-CRM9 is an immunotoxin; "thus, the use of the immunotoxin in humans to inhibit the rejection of kidney transplants was clearly contemplated and in Applicants' possession".

Applicant's argument is noted, however, UCHT1-CRM9 is not the truncated antibody of the instant claims. Further, this daisy-chaining together of pieces of the claimed invention disclosed in unrelated sections of the specification does not comprise an adequate written description.

Applicant argues, "Furthermore, because CRM9 is a full-length toxin moiety and, as shown on page 40, lines 9-32, and the efficacy of a full-length toxin would be inhibited by pre-existing anti-diphtheria toxin antibodies in humans immunized against diphtheria, a truncation mutant of the full-length diphtheria toxin moiety must be used in humans. … Therefore, the use of UCHT1-DT390 or other C-terminal truncation mutants to inhibit transplant rejection were in Applicants' possession".

It remains the Examiner's position that the use of UCHT1-DT390 in the claimed method might be *obvious*, but it is not disclosed in the specification.

Regarding B), Applicant indicates that, "Applicants have again amended claim 48 to track the language of the specification on page 40, lines 28-32 which describes a truncated toxin moiety that bypasses the inhibitory effect of pre-existing anti-diphtheria antibodies".

A review of page 40, lines 28-32 discloses, "A DT point-mutant, a truncation mutant and DT-subfragments were used in an attempt to neutralize the anti-DT effect in human sera. Based on the neutralization data, a single-chain immunotoxin was constructed with a C-terminal deletion mutant of DT which is expected to bypass the inhibitory effect of the pre-existing anti-DT antibodies". This cite comprises part of Example 9, wherein at page 40, lines 28-32 the specific "C-terminal deletion mutant of DT" is not disclosed. This example, wherein a *single, undefined* construct is disclosed, cannot support the generic immunotoxin of the instant claims.

Applicant cites original Claims 4-7.

Original Claims 4-7 do not recite the new limitation of a truncated toxin moiety which bypasses the inhibitory effect of pre-existing anti-diphtheria toxin antibodies. This limitation is disclosed only at page 40 as set forth in the description of the single, undefined construct of Example 9.

6. Claims 31-33, 37, 39, and 44-47 are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from

7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

8. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

11/13/06

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